Magnolia Derived Honokiol and Magnolol Fight Against Skin Inflamm'Aging

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Abstract

In the process of aging, the immune system becomes less effective and its capacity to manage the inflammatory response is reduced. This can lead to chronic inflammation characterized by a slow but continuous production of free radicals. In skin, chronic inflammation causes the known phenomena of skin aging such as wrinkles and loss of elasticity. The term "inflamm-aging" describes this close relationship between inflammation and aging. During this process one of the inflammatory transcription factors, Nuclear Factor-Kappa B (NF-κB), remains active instead of self-regulating its level. The main component of the Magnolia bark extract, magnolol and honokiol, are known to block NF-κB as well as having anti-oxidant and anti-bacterial properties. In a commercial available ingredient these hardly water soluble actives were incorporated into lecithin liposomes for an optimal skin uptake. In clinical studies, the Magnolia based ingredient was shown to reduce redness in facial skin, to restore moisture and to prevent loss of skin elasticity.

Inflammation

In response to tissue injury induced by trauma or infection the inflammatory response sets in, constituting a complex network of molecular and cellular interactions directed to facilitate a return to physiological homeostasis and tissue repair. The response is composed of both local events and a systemic activation mediated by cytokines.

Inflammation evokes inflammatory cells like macrophages, neutrophils, monocytes, to invade at the site of infection. This leads to the release of large amounts of free radicals and the death and degradation of the pathogenic organisms, agent or affected cells. After that, inflammation resolves, the healing step initiates and tissue homeostasis is restored.

If tissue health is not re-established (or in response to stable low-grade irritation), inflammation becomes a chronic condition (1). During chronic inflammation, the immune system persists to produce low levels of the key molecular players such as prostaglandins, cytokines and nuclear factor-κB (NF-κB). This constant supply of free radicals overwhelms our antioxidant defences, damages DNA and therefore ages us (2). In skin, chronic inflammation causes the known phenomena of skin aging such as wrinkles and loss of elasticity, the ultimate cause being the breakdown of collagen and elastin fibers.

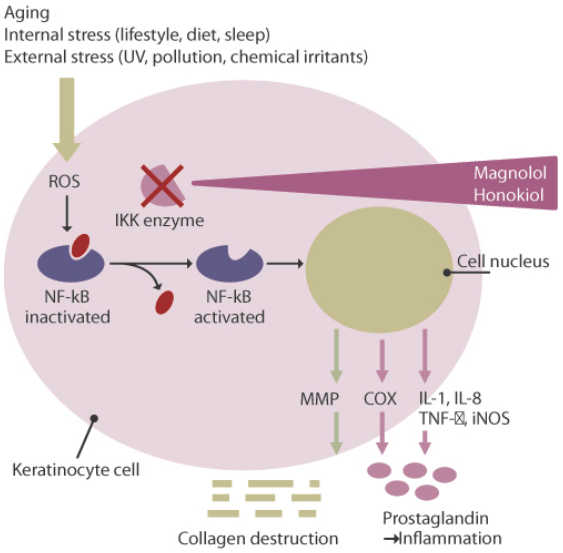

Figure 1 Inhibition of NF-κB. Magnolol and Honokiol block the activation of NF-κB and its activity through the inactivation of the enzyme IKK (IκB kinase).

Aging of the skin is a process with very direct effects on the daily life and psychological and social well-being of an individual. The skin is a major sensory organ, it is the body's first line of defense against infectious organisms and physical harm, and it plays a very important role in controlling body temperature.

Slowing down the aging processes of the skin will therefore not only help us to keep a more youthful appearance but will most likely have beneficial effects for the whole organism.

Inhibition of Inflamm'Aging

The nuclear factor-kappa B is an important transcription factor in the regulation of inflammation; many pro-inflammatory stimuli can activate it. NF-κB exists in a latent state in the cytoplasm bound to specific inhibitory proteins, IκBs (inhibitor of κB). Activation of NF-κB is initiated by the signal-induced degradation of IκB proteins (Figure 1). This occurs via activation of a kinase called the IκB kinase (IKK). When activated, usually by signals coming from the outside of the cell, IKK phosphorylates two serine residues in IκB that will lead to its degradation by the proteasome. NF-κB is now free to enter into the nucleus to regulate the transcription of multiple pro-inflammatory mediator genes and matrix-metalloproteinases (MMP). Finally, NF-κB is turned off by itself.

In the skin, an excess of reactive oxygen species (ROS) can make NF-κB chronically active leading to a continuous release of inflammatory mediators and thus to chronic inflammation. These ROS can be over-generated by aging, external stresses (such as UV, pollution, toxins, chemical irritants) and internal ones (lifestyle, diet, lack of sleep).

Magnolia officinalis is a medicinal plant belonging to the China pharmacopeia and is a natural inhibitor of NF-κB. Its bark has been used for thousands of years in Asia to treat the stagnation of qi (lack of energy) and more precisely digestive disorders, anxiety and allergic diseases. In Japan, two of the most popular herbal medicines used, one called saiboku-to and another called hange-kobuku-to, contain magnolia bark and have been used for treating ailments from bronchial asthma to depression and anxiety.

The two pharmacologically active substances present in the Magnolia bark are called magnolol and honokiol (Figure 2). These two low molecular weight lignans synergistically reduce inflammation by inhibiting NF-κB activation and activity through IKK (κB kinase) enzyme inactivation (3). As a result, there is an inhibition of the production of inducible-nitric oxide synthase (iNOS), interleukine 8 (IL-8), tumor necrosis factor α (TNF-α) and COX-2 (4). Besides, they have antioxidant, anti-bacterial and anti-angiogenic effects and can relieve spasms. Magnolol has also anti-depressive, anti-allergic and anti-asthma effects whereas honokiol is anxiolytic. Japanese researchers have determined that the magnolol and honokiol components of Magnolia officinalis are one thousand times more potent than alpha-tocopherol (vitamin E) in their antioxidant activity (5).

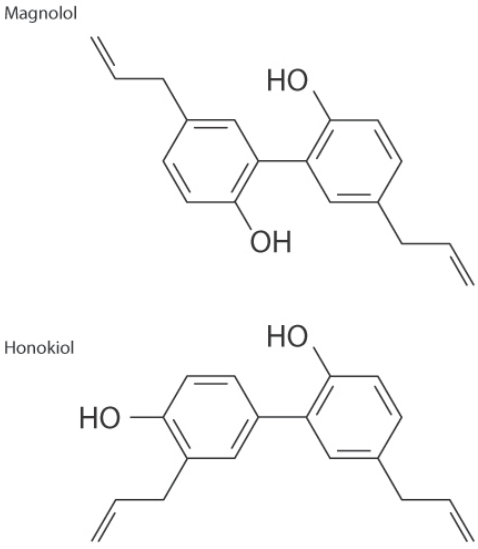

Figure 2 Structures of Magnolol and Honokiol. The low molecular weight lignans identified as the active substances in the Magnolia bark extract.

Preparation of a Cosmetic Ingredient based on Magnolia Bark

Magnolol and honokiol have low solubility in water and it has been necessary to develop a proprietary technique to extract the active substances for use in a water soluble ingredient.

Ethanol and water are used to obtain an extract of the Magnolia bark which is then sprayed onto a carrier of maltodextrin and liposomes. The powder that results (MAXnolia) is free of alcohol and contains pre-liposomes. These pre-liposomes turn into liposomes immediately in contact with water and then the active ingredients are incorporated into the bi-layer membranes.

The process has a number of advantages including the fact that the resulting ingredient is preservative free and alcohol free, with good skin delivery due to the liposomes.

Clinical Studies with an Anti-Inflamm'Aging Formulation

Anti-Redness Effect

A clinical study was performed over 4 weeks with 20 women having visible facial skin redness. A cream comprising 0.5% MAXnolia was applied twice per day on one side of the face and the placebo cream on the other side (vehicle-controlled half side comparison). Skin redness was determined by measuring the parameter a* in the L*a*b* color system using a Chromameter Minolta CR 400 (Minolta, Japan). a* characterizes the color intensity from green to red and an increase of a* indicates an increase of the red constituent of the skin. Results showed that the Magnolia based ingredient significantly reduced half-side facial skin redness compared to the placebo (Figure 3).

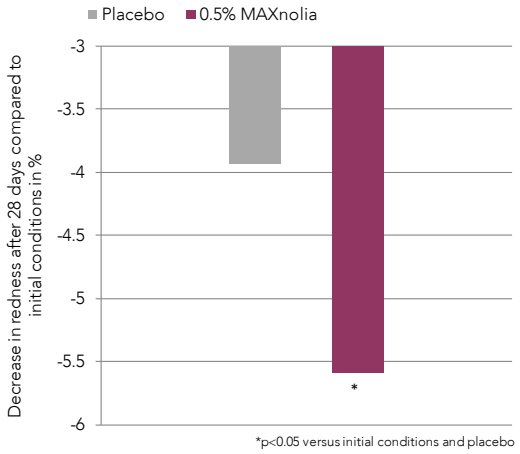

Figure 3 Reduction of Facial Skin Redness after 28 days of treatment with a 0.5% MAXnolia cream in comparison to placebo.

Anti-Ageing Effect on the Crow's Feet Area

The anti-wrinkle efficacy of MAXnolia was demonstrated in a clinical trial over 2 months with 21 volunteers aged from 35 to 58. A cream containing 0.5% of MAXnolia was applied twice per day on the eye contour area. Two parameters were assessed using a Cutometer SEM 575 (Courage & Khazaka): the skin elasticity and the skin fatigue which indicates the loss of elasticity due to repetitive mechanical stresses (skin elasticity tends to decrease with age whereas skin fatigue increases). Results showed that Magnolia extract based cream increased the skin elasticity of the crow's feet and decreased the skin fatigue compared to the placebo (Figure 4).

Improvement of the Skin Quality

To determine a general improvement of the skin in vivo, a cream containing 0.5% of the ingredient was applied to both the face and the inner side of the

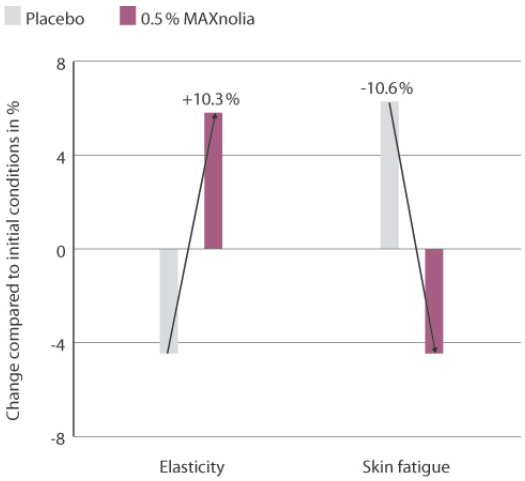

Figure 4 Improvement of the eye contour area. After 28 days application of a cream with 0.5% MAXnolia, skin elasticity increased and skin fatigue was reduced.

forearms of volunteers aged from 54 to 78 over 28 days. Skin hydration and firmness were determined on the inner side of forearms using respectively a Corneometer MPA 5 CPU (Courage+Khazaka GmbH, Cologne) and a Cutometer MPA 580 (Courage+Khazaka GmbH, Cologne). Trans epidermal water loss (TEWL) was measured on the face by means of AquaFlux Model AF200 (Biox Systems Ltd, London, UK).

At day 0 the parameters were determined in the test areas under standardized conditions and the first application of the products was done. From day 1 to 28 the test products were applied twice a day and at day 28 the parameters were measured again. Results showed that the cream containing MAXnolia significantly increased skin hydration and firmness and decreased TEWL compared to the placebo (Figure 5).

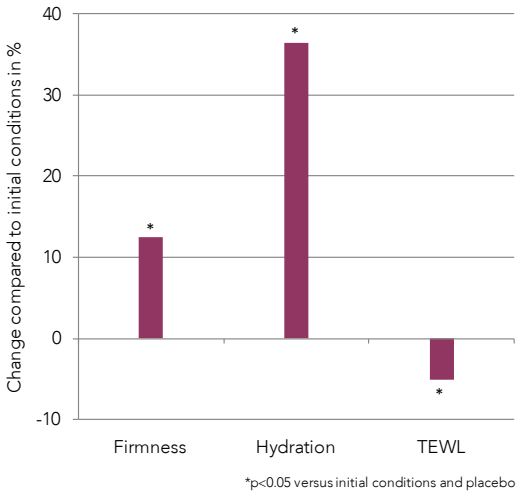

Figure 5 Improvement of skin firmness and hydration after 4 weeks application of a cream containing 0.5% MAXnolia.

Conclusion

The normal, healthy process of tissue repair leads inevitably to the production of large quantities of inflammatory factors while the body gets rid of the damaged or infected tissue before repair can start. However, if this process is left incomplete (more likely to arise in older individuals), chronic inflammation can occur. The inhibition of NF-κB activity by magnolol and honokiol helps to stop the chronic inflammatory process which is linked to the skin's ageing process and the development of lines, wrinkles, blotchiness and reddening of the skin. The results presented in this article show that the Magnolia based ingredient prevents loss of skin elasticity, restores moisture and reduces redness in facial skin. An overall improvement was achieved in the skin quality where the anti-inflammaging ingredient was applied.

References

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